# ABSTRACT

## THE INFLUENCE OF $CaCl_2$ CONCENTRATION AS CROSSLINKER ON PHYSICAL CHARACTERISTICS OF ANDROGRAPHOLIDE NANOCRYSTAL (Prepared by Wet Ball Milling Method)

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Nanocrystals is homogenous drug crystals in nanometer domain stabilized with stabilizer such as carboxymethyl chitosan (CMCS). Crosslinking of CMCS with calcium chloride ($CaCl_2$) enables to prolong drug absorption. It is expected that crosslinking nanocrystals with crosslinker will result in crosslinked nanocrystals with homogenous size and higher entrapment efficiency. This study is aimed to evaluate the influence of $CaCl_2$ concentration on physical characteristics of crosslinked nanocrystals using andrographolide as model compound. 50 mg Andrographolide (Health Ingredients Co.,Ltd,China) was dispersed in 1%(w/v) CMCS (China Eastar Group Co.,Ltd.) then milled with 50 mm milling beads (Hosokawa, Japan) for 24 hours. Nanocrystals formed (F1) was then added with $CaCl_2$ (F2:0,125%(w/v); F3:0,250%(w/v); F4:0,375%(w/v)) and stirred for 1 hour for crosslinking reaction. Nanocrystals formed were analyzed for its particle size, shape, and chemical bond changes. Crosslinked nanocrystals obtained have rough surfaces and irregular shape. X-Ray diffractogram of crosslinked and non-crosslinked nanocrystals shows crystalline peak of andrographolide disappear that means andrographolide dispersed in the system. The particle size of crosslinked nanocrystals (F2: 505,6 ± 7,7 nm; F3: 485,5 ± 9,5 nm; F4: 489,2 ± 10,3 nm) have smaller size than non-crosslinked nanocrystals (F1:512,8 ± 5,3 nm). There is no different between drug recovery of crosslinked and non-crosslinked nanosuspensions. Crosslinking of nanocrystals andrographolide-CMCS with $CaCl_2$ was detected in all concentrations of $CaCl_2$ added and also resulted in smaller particle size. Furthermore, the effectivity of crosslinked nanocrystals for prolonging drug absorption is needed through release study.

**Keywords:** Nanocrystal, wet ball milling, andrographolide, carboxymethyl chitosan, $CaCl_2$